

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
31 May 2001 (31.05.2001)

PCT

(10) International Publication Number
WO 01/38324 A3

(51) International Patent Classification: C07D 401/04,
A61K 31/4178, A61P 43/00, C07D 401/14, 417/14,
409/14, 403/04

[GB/GB]; SmithKline Beecham Pharmaceuticals, New
Frontiers Science Park South, Third Avenue, Harlow,
Essex CM19 5AW (GB).

(21) International Application Number: PCT/GB00/04413

(74) Agent: BLAKEY, Alison, Jane; SmithKline Beecham,
Corporate Intellectual Property (CN9.25.1), 980 Great
West Road, Brentford, Middlesex TW8 9GS (GB).

(22) International Filing Date:

20 November 2000 (20.11.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

| | | |
|------------|-------------------------------|----|
| 60/166,814 | 22 November 1999 (22.11.1999) | US |
| 60/166,886 | 22 November 1999 (22.11.1999) | US |
| 60/166,885 | 22 November 1999 (22.11.1999) | US |
| 60/166,895 | 22 November 1999 (22.11.1999) | US |

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*):
SMITHKLINE BEECHAM P.L.C. [GB/GB]; New
Horizons Court, Brentford, Middlesex TW8 9EP (GB).

Published:

— with international search report

(72) Inventors; and

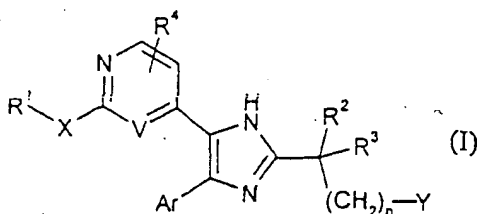
(75) Inventors/Applicants (*for US only*): DEAN, David,
Kenneth [GB/GB]; SmithKline Beecham Pharmaceu-
ticals, New Frontiers Science Park South, Third Avenue,
Harlow, Essex CM19 5AW (GB). LOVELL, Peter, John
[GB/GB]; SmithKline Beecham Pharmaceuticals, New
Frontiers Science Park South, Third Avenue, Harlow,
Essex CM19 5AW (GB). TAKLE, Andrew, Kenneth

(88) Date of publication of the international search report:
10 May 2002

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

WO 01/38324 A3

(54) Title: IMIDAZOLE DERIVATIVES AND THEIR USE AS RAF KINASE INHIBITORS



(57) Abstract: Compounds of formula (I) wherein X is O, CH₂,
S or NH, or the moiety X-R¹ is hydrogen; V is CH or N; Y is
NR¹⁰R¹¹, NR¹⁰C(Z)NR¹⁰R¹¹, NR¹⁰COOR¹¹ or NR¹⁰SO₂R¹¹; Ar is
phenyl or a 5- or 6-membered heteroaryl ring either of which may
be optionally substituted; n is 0, 1, 2, 3 or 4; and R¹, R², R³, R⁴,
R¹⁰ and R¹¹ have the meanings given in the description; and phar-
maceutically acceptable salt thereof.

INTERNATIONAL SEARCH REPORT

Inter. Application No
PCT/GB 00/04413

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D401/04 A61K31/4178 A61P43/00 C07D401/14 C07D417/14
C07D409/14 C07D403/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | WO 99 32436 A (BAYER CORPORATION) 1 July 1999 (1999-07-01) page 2; claim 1 --- | 1,12,13 |
| A | WO 99 32455 A (BAYER CORPORATION) 1 July 1999 (1999-07-01) page 2; claim 1 --- | 1,12,13 |
| A | WO 99 01449 A (NOVARTIS AG) 14 January 1999 (1999-01-14) cited in the application page 20; example 18 --- | 1,12 |
| P,A | WO 00 26209 A (NOVARTIS AG) 11 May 2000 (2000-05-11) cited in the application page 28; examples 10,12-15 --- -/-- | 1,12 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

5 June 2001

Date of mailing of the international search report

18/06/2001

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

Inter. Application No
PCT/GB 00/04413

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| P, A | WO 99 61437 A (SMITHKLINE BEECHAM CORPORATION) 2 December 1999 (1999-12-02) claims ----- | 1, 12 |

BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Application No

PCT/GB 00/04413

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| WO 9932436 A | 01-07-1999 | AU 1905499 A | 12-07-1999 |
| | | BG 104599 A | 30-03-2001 |
| | | CN 1283180 T | 07-02-2001 |
| | | DE 1049664 T | 03-05-2001 |
| | | EP 1049664 A | 08-11-2000 |
| | | ES 2153809 T | 16-03-2001 |
| | | NO 20003230 A | 21-08-2000 |
| | | TR 200002616 T | 21-11-2000 |
| WO 9932455 A | 01-07-1999 | AU 1905599 A | 12-07-1999 |
| | | BG 104598 A | 28-02-2001 |
| | | CN 1283192 T | 07-02-2001 |
| | | EP 1056725 A | 06-12-2000 |
| | | ES 2155045 T | 01-05-2001 |
| | | NO 20003231 A | 22-08-2000 |
| | | TR 200002617 T | 21-11-2000 |
| WO 9901449 A | 14-01-1999 | AU 8801598 A | 25-01-1999 |
| | | BR 9810955 A | 26-09-2000 |
| | | CN 1261885 T | 02-08-2000 |
| | | EP 0993456 A | 19-04-2000 |
| | | NO 996429 A | 23-12-1999 |
| | | PL 337057 A | 31-07-2000 |
| | | SK 186599 A | 12-06-2000 |
| | | TR 9903278 T | 21-07-2000 |
| | | ZA 9805656 A | 30-12-1998 |
| WO 0026209 A | 11-05-2000 | AU 6476599 A | 22-05-2000 |
| WO 9961437 A | 02-12-1999 | AU 4195999 A | 13-12-1999 |
| | | BR 9910621 A | 30-01-2001 |
| | | EP 1080087 A | 07-03-2001 |
| | | NO 20005878 A | 21-11-2000 |

BEST AVAILABLE COPY